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Current concepts in pancreatic cancer: symposium summary.

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This recent symposium featured speakers from several clinical and research disciplines. Among the findings: peptic ulcer disease is a significant predisposing risk factor (odds ratio = 3.9) for pancreatic cancer; as many as 50% of all intraductal papillary mucinous neoplasms are associated with invasive adenocarcinomas; alteration of gene expression via methylation of a gene promotor region constitutes a potentially reversible method of tumor suppressor gene inactivation; > 400 transcriptional alterations of gene expression have been identified for pancreatic cancer; some common molecular markers such as p53 and HER-2/neu may be related to morphologic alterations of in situ neoplasia and to transcriptional alterations of gene expression rather than mutational events; epidermal growth factor (EGF), transforming growth factor beta (TGF-beta), and related molecules may modulate gene transcription via "autocrine" or "paracrine" mechanisms; several cytokines, amylin (islet amyloid polypeptide), and other cachexia factors are responsible for paraneoplastic peripheral insulin resistance, ineffective utilization of glucose, and profound cachexia. In the clinical diagnostic arena: the World Health Organization established a standard nomenclature for intraductal papillary mucinous neoplasms, mucinous cystic tumors, intraductal mucinous hyperplasias, and solid pseudopapillary tumors; focal glandular differentiation may be commonly identified within pancreatic endocrine neoplasms (islet cell tumors) while not necessarily implying an unfavorable prognosis typical of ductal adenocarcinomas; positron emission tomography scanning may be used for evaluation of early tumor response to novel chemotherapeutic regimens; helical computed tomography (CT) is the state of the art in preoperative imaging for pancreatic cancer; neoadjuvant 5-fluorouracil (5-FU)-based chemoradiation in 39 "resectable" patients provided a median survival of 19 months, actuarial 4-year survival of 19%, and improved local tumor control; gemcitabine has shown promise in alleviating tumor-related symptoms with a significantly better "clinical benefit response" than single agent 5-FU (23.8 vs. 4.8%, p = 0.0022) based on change in pain intensity, daily analgesic consumption, performance status, and weight; a significant survival advantage was demonstrated in patients treated with conventional therapies whose tumors expressed p21WAF-1, an important inhibitor of cell cycle progression and downstream molecule of p53 and TGF-beta; a p21-adenovirus (rAD-p21) gene therapy resulted in significant growth inhibition of pancreatic cancer cell lines in tissue culture, and development of a successful SCID mouse-human pancreatic adenocarcinoma xenograft model provided an animal model for preclinical trials of rAD-p21.

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